

Claims

1. Method for culturing cells in order to produce substances characterized in that, a cell producing substances is cultured under glucose limitation (DGL), wherein the DGL ($DGL = qGlc/qGlc_{max}$ where $qGlc$ = observed current specific glucose consumption rate and $qGlc_{max}$ = maximum known specific glucose consumption rate for these cells) is larger than the DGL which only leads to the maintenance ($DGL_{maintenance}$) of the cell and is ≤ 0.5 , wherein $DGL_{maintenance} = qGlc_{maintenance}/qGlc_{max}$ where $qGlc_{maintenance}$ = the observed specific glucose consumption rate for pure maintenance metabolism and $qGlc_{max}$ = maximum known specific glucose consumption rate for these cells.
2. Method as claimed in claim 1, characterized in that the DGL is ≤ 0.4 or ≤ 0.3 .
3. Method as claimed in claim 1 or 2, characterized in that the amount of fed glucose is not more than 50 % of that which can be maximally consumed by the maximum expected cell count without glucose limitation.
4. Method as claimed in claim 3, characterized in that the amount of fed glucose is not more than 35 % of that which can be maximally consumed by the maximum expected cell count without glucose limitation.

5. Method as claimed in one of the claims 1 to 4,
characterized in that
one component is used from the group of cell lines comprising CHO such as
CHO-K1, BHK such as BHK-21, hybridoma, myeloma cells such as NS/O,
other mammalian cells and insect cells or other higher cells.

6. Method as claimed in one of the claims 1 to 5,
characterized in that
the produced substances are proteins or polypeptides.

7. Method as claimed in claim 6,
characterized in that
the produced substances are fusion proteins, MUC1-IgG2a, MUC2-GFP-C-term,
EPO, interferons, cytokines, growth factors, hormones, PA, immuno-globulins, fragments of immunoglobulins or other glycoproteins.

8. Method as claimed in one of the claims 1 to 7,
characterized in that
a glucose-containing medium is used which is not limiting with regard to
other nutrient components before glucose limitation occurs.

9. Method as claimed in claim 8,
characterized in that
the glucose is fed separately from other substrates.

10. Method as claimed in one of the claims 1 to 9,
characterized in that
it is carried out in a pH range of 6.7 – 7.7.

11. Method as claimed in one of the claims 1 to 10,
characterized in that
it is carried out in a temperature range in which irreversible destruction of
the product does not occur.

12. Method as claimed in one of the claims 1 to 11,
characterized in that
it is operated in a continuous process with at least partial cell retention.

13. Method as claimed in one of the claims 1 to 12,
characterized in that
it is carried out in a fed-batch process.

14. Method as claimed in one of the claims 1 to 13,
characterized in that
it is started as a batch and continued as a fed-batch or continuous process.

15. Method as claimed in one of the claims 1 to 14,
characterized in that
it is carried out with cells whose production is not coupled to growth.